REMARKS

Claims 1-2, 4-5, 7-12, 14-21 are pending in the application. Of the pending claims, Claims 11 and 12 are withdrawn. Independent Claims 1 and 17 are amended to further define Applicant's invention as a drug-containing layered structure with water-swellable gel-forming outermost layers with a film-forming agent that gels when in contact with moisture to facilitate swallowing of the orally administered agent and that releases the drug in the digestive tract. Support for these amendments can be found in the specification on page 3, lines 12-27 and continuing on page 4, lines 1-10, page 9, lines 14-20, and page 10, last paragraph continuing to page 11.

Claim 2 is amended to better define Applicant's claimed invention as a film-shaped preparation formable into a plurality of configurations with an adjustable film-forming agent that facilitates swallowing of the orally administered agent and that releases the drug in the digestive tract so that the drug-containing layer does not dissolve in the mouth. Support for this amendment can be found throughout the specification, for example, on page 9, lines 6-20, and page 16 lines 11-25. Claims 4 and 5 are amended to more clearly define Applicant's claimed invention. Claim 16 recites that the water-swellable gel-forming layer facilitates swallowing of the orally administered agent and prevents the drug-containing layer from dissolving in the mouth.

The Advisory Action dated February 13, 2009 noted that the information disclosure statement filed on November 11, 2008 was noncompliant under 37 CFR 1.97(c) and therefore placed in the application but the information referred to therein has not been considered. Applicant will file a fully compliant supplemental disclosure statement.

Reconsideration of the present application is respectfully requested.

Claim Rejections - 35 USC §103

In the Final Office Action dated September 9, 2008, Claims 1-2, 4, 5, 7-10 and 14-16 were rejected under 35 U.S.C. §103(a) as being unpatentable over Yamamura (Yamamura). The Examiner provided further remarks regarding this rejection in the Advisory Action dated February 13, 2009. This rejection is respectfully traversed for the following reasons.

The presently claimed orally administered agent is patentably distinct from the multi-layered film in Yamamura. Yamamura discloses a triple-layered film comprising an adhesive layer, an intermediate drug-containing layer and a top layer made difficult to dissolve in water (non-adhesive layer) (col. 2 lines 11-17). In some cases the adhesive layer is combined with the drug layer (col. 2 line 14). The purpose of the adhesive layer is to affix or provide steady application to a mucous membrane in an oral cavity. The adhesive layer should not come off by movement of the mucous membrane (cheek) and does not move easily by force of tongue (col. 14 lines 15-18). The adhesive layer of the final product of Yamamura is in the form of a powder (col. 3 lines 19-20). The non-adhesive top layer covers the intermediate drug-containing layer and the lower adhesive layer. The top layer is difficult to dissolve in water and secures the drug layer next to the mucous membrane, thereby preventing digestion since the drug-containing layer does not dissolve in the mouth.

Applicant respectfully asserts the presently claimed invention is patentably distinct from the teachings of Yamamura since Yamamura's drug-containing film:

- is *not free of a bioadhesive layer* as in Applicant's Claims 1, 2-10, 14-16 and 19; rather Yamamura's film is structured to *adhere* to the mucous membrane in an oral cavity;

- is not *swallowed* as in Applicant's Claims 2, 16 and 21; rather Yamamura's film is structured to deliver the drug whiled being stationary and adhered to the inside of the oral cavity much in the same way as a band aid functions; and

- is not *water-swellable gel-forming layers with a film-forming agent covering a drug-containing layer(s) where the gel-forming layers gel upon contact with moisture to mask odor, facilitate swallowing and ingestion of the drug in the digestive tract without dissolving in the mouth* (See Applicant's Claims 1, 7, 16, 17 and 19-21); rather Yamamura's film is structured to resist permeability of moisture enabling it to remain adhered to the moist, mucous membrane of the oral cavity and not to be swallowed.

Applicant respectfully asserts that because Yamamura does not teach Applicant's claimed orally administered agent, there is no reason for one skilled in the art to use the teachings of Yamamura for an orally administered agent as presently claimed.

Further, the Examiner argues on page 8, lines 10-13 of the Office Action that:

> "Adhesive substance include (sic) carboxyvinyl polymer and its pharmaceutically acceptable non-toxic salts. These compounds (sic) provided excellent adhesion when such a substance was applied on the drug containing layer (col. 5 lines 5-17)."

As described above, the goal of Yamamura is adhesion of the disclosed film preparation to the mucous membrane. The formulas and combination of chemicals in the Yamamura preparation are for that specific purpose. Applicant's Claim 5 recites a *carboxyvinyl polymer cross-linked by a polyvalent metal compound* for holding the drug-containing layer within the *first and second water-swellable gel-forming layers.* The presently claimed agent does not adhere to the mucous membrane, but rather provides two water-swellable gel-forming layers that swell through moisture in saliva or the like in the mouth of a patient to form a gel that changes into a form having a size, shape, elasticity, viscosity so that swallowing is easy for the patient.

The cross-linked carboxyvinyl polymer of Applicant's claimed invention is structurally distinct from that of Yamamura. One of ordinary skill in the art would have no reason to use the teachings of Yamamura to crosslink carboxyvinyl polymer with a metal compound to formulate an orally administered agent that is easily swallowable.

For the foregoing reasons, Applicant respectfully asserts the teachings of Yamamura do not provide reason for a skilled artisan toward the invention as set forth in the presently claimed invention. *United States* v. *Adams*, 383 U.S. 39, 40 (1966); ***KSR Int'l** v. Teleflex Inc.*, 127 S. Ct. 1727, 1740-41, 82 USPQ2d 1385, 1396 (2007).

Further, the Final Office Action mailed on September 9, 2008 identifies on page 9, first paragraph the elements in the present application that are not included in the adhesive layer of Yamamura. As explained repeatedly by USPTO Board of Appeals and Interferences and elsewhere in the case law, a reference cannot be properly modified if the effect would be to destroy the invention on which the referenced patent is based. *Ex parte Hartmann*, 186 USPQ 366 (P.T.O.Bd.Ap. 1974); *Ex parte Thompson*, 184 USPQ 558 (P.T.O.Bd.Ap. 1974). See also ***In** re Rosen* 213 USPQ 347 (CCPA) 1982; and *In re Dembiczak,* 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999). The elements that are absent in the teachings of Yamamura represent significant modifications that destroy the presently claimed agent as recited by Applicant.

The Examiner concludes on page 9, last paragraph of the Final Office Action that:

> "It would have been obvious to one of ordinary skill in the art to utilize carboxyvinyl polymer in both layers surround the drug containing layer. One of ordinary skill in the art would have been motivated to add this adhesive agent as it is taught by Yamamura et al. as providing excellent adhesion when applied to the drug-containing layer. By having the adhesive component in both layers, adhesion to the drug-containing layer can be achieved."

In the quote cited above, the Examiner has suggested that the ordinary artisan would have modified the layer made difficult to dissolve in water (non-adhesive layer). Applicant strongly disagrees that modification of this layer is obvious at all. Applicant's carboxyvinyl polymer is crosslinked with a metal compound and the adhesive layer and other layers secure the drug-containing layer encapsulated within a first and second water-swellable gel-forming layers made easy to dissolve in moisture, mask ordor, and facilitate swallowing. In contrast, Yamamura teaches the use of a carboxyvinyl polymer for an adhesion of a drug-containing film to the moist membrane of an oral cavity that is immovable and highly impermeable to moisture. The formulation of the carboxyvinyl compound is not stated as crosslinked with a metal compound and is obviously intended to serve very different functions from the presently claimed invention. This is further supported in that Yamamura does not teach the percentages and formulation comprising polyvinyl alcohol as admitted in the Final Office Action on page 9, first paragraph.

While in the presently claimed agent, the first and second layers may have a similar function, Yamamura clearly describes different functions for each layer. Also, it is unclear as to what reason the ordinary artisan would have had to modify the non-adhesive layer at all, and particularly the modification suggested by the Examiner, as such modification may disrupt the important functions these layers are intended to provide in the presently claimed invention.

Further, the film adhesion disclosed in Yamamura is different from applicant's claimed invention. Applicant respectfully asserts that the Examiner is making a conclusion about adhesion of the layers of the film to *each other* while the teachings of Yamamura use the term adhesion to refer to adhering the film to the mucous membrane. The ordinary artisan would have no reason to modify any compositions of the layers of the film of Yamamura because adhesion of the film of Yamamura to the mucous membrane would have been adversely affected if the layers were modified as suggested by the Examiner.

The preamble of the presently pending claims recites "an orally administered agent free of a bioadhesive layer." Yamamura contains a bioadhesive layer that adheres to a mucous membrane in the oral cavity. Contrarily, the presently claimed invention is directed to solving problems unique to an orally administered agent containing a drug. It is well established in the case law that if a limitation in the preamble of a claim necessarily gives meaning to the claim and properly defines the invention, then such limitation must be considered when determining the patentability of the claims. The predecessor court of the Court of Appeals for the Federal Circuit (CAFC), namely, the Court of Custom and Patent Appeals (CCPA), summarized this approach in *Kropa v. Robie,* 88 USPQ 478(1951), after reviewing some 37 cases that turned on the limiting nature of the preambles to the claims in suit. See also *Loctite Corp v. Ultraseal Ltd.,* 228 USPQ 90, 94 (Fed. Cir. 1985). According to the court in Kropa:

> "[T]he preamble has been denied the effect of a limitation where ... the claim or [interference] count apart from the introductory clause completely defined the subject matter [of the invention], and the preamble merely stated a purpose or intended u se of that subject matter. On the other hand, in those... cases where the preamble to the claim our count was expressly or by necessary implication given the effect of a limitation, the introductory phrase was deemed essential to point out the invention defined by the claim or eount. In the latter class of cases, the preamble was considered neecssary to give life, meaning and vitality to the claims or counts."

Examples of preambles cited in *Kropa* as expressly or impliedly help to express a limitation in the claims are "An insecticide" and "An insecticidc composition." Applicant respectfully asserts that the claims in this application present precisely the situation where the preamble of a claim has been held to express a limitation in the claim in *Kropa.* The preamble of applicant's claims distinguishes the presently claimed invention by defining an orally administered agent free of a bioadhesive layer, which area of technology is unique and presents significantly more difficulties compared to, for example, the film applied to a mucous

membrane, such as that proposed by Yamamura Therefore, Applicant respectfully asserts that teachings that are not concerned with an orally administered agent free of a bioadhesive layer, such as that of Yamamura, could not possibly give reason to one of ordinary skill in the art to the presently claimed orally administered agent.

Based on the foregoing arguments, applicants submit that the present claimed agent is patently distinguishable from the teachings of Yamamura.

In the Final Office Action dated September 9, 2008, Claims 17-21 were rejected under 35 U.S.C. §103(a) as being unpatentable over Takayanagi et al . (Takayanagi), in view of Kuroya et al. (Kuroya) and Geoghegan et al. (Geoghegan). This rejection is respectfully traversed for the following reasons.

The present invention as recited in Claims 17-21 is drawn to an agent with multiple drug-containing layers that are heat-sealed via an intermediate layer which includes a heat-sealing adhesive. The agent has a water-swellable gel-forming layer as an outermost layer.

Takayanagi discloses adhesive medical tapes for oral mucosa, having a support layer composed of an intestine-soluble polymer, and a medicament-containing layer composed of a water-soluble polymer containing drug. The purpose of the support layer is to prevent the form of the adhesive medical tape from being collapsed or deformed (col. 3 lines 50-53). The Examiner has noted that the medicament layer is preferably composed of two or more layers. However, Takayanagi also describes at col. 4 lines 27-31 that "[i]n case to two medicaments layers a solution which is obtained by dissolving the components of the second medicament layer in the solvent is spread on the first medicament layer and dried to form a second medicament layer." Therefore, Takayanagi fails to teach or suggest two medicament-containing layers with an intermediate layer therebetween.

The Examiner has admitted that Takayanagi fails to disclose medicament layers comprising polyvinyl acetate. In order to cure the defects of Takayanagi, the Examiner has added the teachings of Kuroya and Geoghegan. Kuroya is also directed to a film intended for use in the oral cavity. Kuroya discloses a drug preparation having a film "excellent in shape retention on water absorption, and adhesive to the oral mucosa for an extended time" (col. 2, lines 28-30). However, Kuroya fails to disclose multiple medicament layers and does not disclose the presently claimed heat-sealing adhesive containing intermediate layer. Therefore, the combined teachings of Kuroya and Takayanagi fail to disclose the presently claimed invention.

The teachings of Geoghegan are added as diselosing pharmaceutical formulations where after coating, the product is transferred to a tray drying oven for drying. The heating in the methods of Geoghegan is for *drying*, not for *heat-sealing* two layers to each other. Since the pharmaceutical formulation disclosed by Geoghegan is of a different form (a 24 hour controlled release table containing homogeneous spheres of drug) than the tape of Takayanagi or Kuroya, the ordinary artisan would have no reason to use the drying method of Geoghegan since the drying methods disclosed in Kuroya (col. 4 line 63-65) are more applicable to an adhesive tape type medicament.

The Examiner concludes that combining the teachings of Takayanagi with Kuroya and Geoghegan provides a film with better shape retention and long-term use in the oral cavity, and that it would have been obvious to utilize a drying oven to dry the resulting film. Applicant strongly disagrees for the following reasons. The presently claimed orally administered agent is free of a bioadhesive layer. Therefore the film of the present invention does not adhere to a mucous membrane as would the films of Takayanagi, Kuroya and Geoghegan. Further, one skilled in the art would have no reason to combine the references to obtain a multilayer film

heat-sealed to each other via an intermediate layer that includes a heat-sealing adhesive as recited in Claims 17-21. The cited references, taken alone or together, fail to disclose either an intermediate layer between multiple drug layers or an intermediate layer including a heat-sealing adhesive therein.

To clarify, Takayanagi and Kuroya use the term adhere to discuss the relationship between the medicament containing tape and a mucous membrane. Adhesion is desired between the medical tape and the mucous membrane. This teaches away from the present invention where the outermost layer is a water-swellable gel-forming layer that, upon introduction of moisture as saliva or the like in the mouth of a patient to form a gel that changes into a form having a size, shape, elasticity, viscosity so that swallowing is easy for the patient. Adherence to mucosa is not desired. The presently claimed invention uses the term adhere to refer to layers of the agent to other layers, as in the multiple drug-containing layers are adhered to each other via a heat-sealing adhesive found in an intermediate layer between the drug-containing layers.

The claimed invention, wherein "the multiple drug-containing layers are heat-sealed via an intermediate layer which includes a heat-sealing adhesive" is distinguishable from the medical adhesive tape of Takayanagi, even taken in combination with Kuroya and Geoghegan, which teaches drying a first medicament layer on top of another. Firstly, the claims recite an intermediate layer between the drug layers. Secondly, drying one layer on top of another, either through air or oven drying, is a different process from heat sealing with a heat-sealing adhesive.

Further, as discussed above, the preamble of the present claims recites "an orally administered agent free of a bioadhesive layer." Takayanagi contains a bioadhesive layer, the adhesive layer intended to adhere to a mucous membrane in the oral cavity. Contrarily, the presently claimed invention is directed to solving problems unique to an orally administered

agent containing a drug. As argued previously, it is well established in the case law that if a limitation in the preamble of a claim necessarily gives meaning to the claim and properly defines the invention, then such limitation must be considered when determining the patentability of the claims. The preamble of applicant's claims distinguishes the presently claimed invention by defining an orally administered agent free of a bioadhesive layer, which area of technology is unique and presents significantly more difficulties compared to, for example, the film applied to a mucous membrane, such as proposed by Takayanagi, Kuroya and Geoghegan. Therefore, Applicant respectfully submits that the teachings of Takayanagi, Kuroya and Geoghegan, alone or in combination, are not concerned with an orally administered agent free of a bioadhesive layer and an artisan would have no reason based thereon to contemplate the presently claimed invention.

Applicant respectfully submits that the combination of Takayanagi, Kuroya and Geoghegan teaches away from the presently claimed invention and therefore cannot contemplate or suggest the inventions set forth in the present claims. If one did combine the teachings of Takayanagi, Kuroya and Geoghegan, the ordinary artisan would have obtained an adhesive medical tape with medicament layers as taught by Takayanagi comprising polyvinyl acetate as taught by Kuroya and dried in an oven at 50°C as taught by Geoghegan. This combination of references still discloses at best a modified adhesive medical tape. Takayanagi, Kuroya and Geoghegan teach away from formulating a film that is easily swallowable because the intended use of the tape is adherence to a membrane in the oral cavity. Takayanagi, Kuroya and Geoghegan also teach away from a multilayer medicament containing an intermediate layer between the drug-containing layers because the reference discloses placing one layer directly upon another and drying and no teaching suggestion or motivation is provided in Takayanagi, Kuroya or Geoghegan for altering this drug layering pattern. *United States* v. *Adams,* 383 U.S.

39, 40 (1966); *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1740-41, 82 USPQ2d 1385, 1396 (2007).

In view of the foregoing, applicant respectfully submit that this application is in condition for allowance. A timely notice to that effect is respectfully requested.

Please charge any unforeseen fees that may be due to Deposit Account No. 50-1147.

Respectfully submitted,

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